Preparation of a novel composition-gradient thermosensitive gel

Hideaki Tokuyama[1], Masahiro Sasaki[2] and Shuji Sakohara[2]

[1]Department of Chemical Engineering, Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya, 464-8603, Japan

[1]Corresponding information

TEL: +81-52-789-3391, FAX: +81-52-789-3269,

E-mail: htoku@nuce.nagoya-u.ac.jp

[2]Department of Chemical Engineering, Graduate School of Engineering, Hiroshima University, 1-4-1 Kagamiyama, Higashi-Hiroshima, 739-8527, Japan

Abstract

The feasibility of a novel composition-gradient copolymer gel, in which the composition gradually changes with the distance, was examined. The slab-shaped copolymer gels of a thermosensitive primary component, *N*-isopropylacrylamide (NIPA), and an ionic secondary component, 2-acrylamido-2-methyl-1-propanesulfonic acid (AMPS) or acrylic acid (AA), were prepared between two substrates of hydrophilic glass and hydrophobic polytetrafluoroethylene (Teflon). In the NIPA-*co*-AMPS gels prepared at 40°C between glass and Teflon, the content of AMPS gradually decreased toward Teflon wall. The formation of the gradient composition can be attributed to the repulsion of hydrophilic AMPS to Teflon. The composition-gradient NIPA-*co*-AMPS gel bended and stretched reversibly without breaking in response to the change in

temperature. On the other hand, in the NIPA-*co*-AA gels prepared at 40°C between glass and Teflon, AA distributed homogeneously. The difference in the distributions of ionic components in NIPA-*co*-AA and NIPA-*co*-AMPS gels comes from the differences in the reactivities and interactions of the ionic components with NIPA. The conversion of ionic components and the rate of gelation of NIPA-*co*-AA are larger than those of NIPA-*co*-AMPS. The glass transition temperatures of NIPA-*co*-AA gels are higher than those of NIPA and AA gels. This fact is attributed to that NIPA and AA in the copolymer gels are strongly interacting by hydrogen bonding with amide and carboxylic groups. The essential points to prepare a composition-gradient copolymer gel are that in addition to the repulsion to a substrate the secondary component has little interaction with the primary component.

Keywords: thermosensitive gel, *N*-isopropylacrylamide, copolymerization, porous gel, glass transition temperature

1. Introduction

Stimuli-sensitive hydrogels change their physical properties and structures in response to external stimuli such as temperature, pH, specific ion, light and electric field. Those so-called intelligent gels have attracted a great deal of attention for their potential applications to actuator, drug delivery system, sensor and so on. One of the methods to develop those high-performance devices is an assembling of polymers having different properties or structures. Iizawa *et al*. [1] reported a gel capsule containing a thermosensitive shell and hydrophilic core portions prepared by the method of amidation of poly(acrylic acid) salt with isopropylamine. Kishi *et al*. [2] reported a

bimetal-like gel containing macroporous and homogeneous layers of thermosensitive poly(vinyl methyl ether) hydrogels prepared by the method of electron beam irradiation. The two types of gels assembled mentioned above have on/off switch-like thermosensitivity. On the contrary, a novel composition-gradient copolymer gel, in which the composition gradually changes with the distance, is expected to show the "buffered" thermosensitivity.

In this study, the preparation of the novel composition-gradient copolymer gel was investigated. We will focus on the preparation method based on the hydrophilic and hydrophobic properties of polymers and substrates. The effects of hydrophilicity and hydrophobicity of substrates on a gelation have been reported. Kato *et al*. [3] reported that thermosensitive poly(*N*-isopropylacrylamide) gels prepared on the surface of hydrophobic polytetrafluoroethylene (Teflon) matrix had cracks on the surface, resulting in the acceleration of deswelling rate. Osada *et al*. [4,5] reported that when vinyl monomers, e.g. 2-acrylamido-2-methyl-1-propanesulfonic acid, in an aqueous solution was polymerized on a hydrophobic substrate, e.g. Teflon, the heterogeneity appeared in the vicinity of the interface.

In this paper, the feasibility was examined for the preparation of composition-gradient copolymer gels composed of a thermosensitive primary component, *N*-isopropylacrylamide (NIPA), and an ionic secondary component, 2-acrylamido-2-methyl-1-propanesulfonic acid (AMPS) or acrylic acid (AA), i.e., NIPA-*co*-AMPS or NIPA-*co*-AA gels. The chemical structures of NIPA, AA and AMPS are illustrated in Fig. 1. Poly(NIPA) has been studied widely as a thermosensitive polymer, having lower critical solution temperature (LCST) in the vicinity of 32°C [6,7], i.e. showing hydrophilicity and hydrophobicity in water at lower and higher temperature, respectively. The gels were prepared between two substrates

of hydrophilic glass and hydrophobic Teflon at various temperatures and concentrations of ionic components. The distribution of the composition in copolymer gels is discussed in terms of the conversion, the rate of gelation and the glass transition temperatures of the copolymer gels.

2. Experimental

2.1. Preparation of gels

NIPA, kindly supplied from Kohjin Co., was purified by recrystallization from hexane and AA was distilled prior to use to remove inhibitor. AMPS was used without further purification. The NIPA-*co*-AMPS and NIPA-*co*-AA gels were prepared by free radical copolymerization. The materials and the corresponding concentrations used were as follows: NIPA-*co*-AMPS or NIPA-*co*-AA ([NIPA] + [ionic component] = 1500 mol/m^3), *N*,*N*'-methylenebisacrylamide of cross-linker (60 mol/m^3), *N*,*N*,*N*',*N*'-tetramethylethylenediamine of accelerator (10 mol/m^3) and ammonium peroxodisulfate of an initiator (1 mol/m^3). The polymerization was performed in water at 20, 25 and 40°C under a nitrogen atmosphere for 24 hours.

The slab-shaped copolymer gels (60 x 60 x 5 mm^3) were prepared by putting pre-gel solution between two substrates of G-G, G-T or T-T, where G and T denote glass and Teflon, respectively. The cylindrical-shaped copolymer gels were also prepared in a glass tube with 14 mm i.d. and were used for measuring glass transition temperature of the gel.

2.2. Measurement of content of ionic component in copolymer gels

The contents of ionic components in copolymer gels were determined by means of the neutralization with NaOH aqueous solution. The slab-shaped gels were cut at 1.0 mm intervals in a direction perpendicular to the substrates. The sliced gels were washed with more than 100 times the gel volume of deionized water for one week. The water was exchanged with the fresh one everyday. Then those were dried in an oven under vacuum at 50°C for 24 hours. The dried gels (0.0044 – 0.348 g) were put in 50 cm^3 of 0.002 $kmol/m^3$ NaOH aqueous solution. After the equilibrium, 5 cm^3 of outer solution were taken out and titrated with 0.001 $kmol/m^3$ HCl aqueous solution to determine the amount of Na ions remaining in the solution. The contents of ionic component in the sliced gels were calculated by the mass balance of Na ions under the assumption that the difference in the amounts of Na ions of initial and equilibrated solutions is equal to the amount of ionic component in gels.

2.3. Measurement of glass transition temperature of gels

The glass transition temperatures, T_gs, of the gels were determined using a differential scanning calorimeter (DSC-60, Shimadzu Co.). The dried cylindrical-shaped gel was used as a sample. An aluminum cell with a sample gel of about 5 mg was sealed and heated up from room temperature to 250°C at a constant heating rate of 5°C/min. The value of T_g was determined as the intersection point of two asymptotic lines at any two points surrounding the inflection point of the DSC curve by using a computer combined with the calorimeter.

3. Results and discussion

Figure 2 shows the contents of AMPS in slab-shaped NIPA-*co*-AMPS gels against the position between G-T, G-G or T-T. The gels were prepared at 40°C under the conditions that the concentrations of NIPA and AMPS were 1455 and 45 mol/m^3, respectively. In the gel prepared between G-T, the content of AMPS gradually decreased toward Teflon wall, i.e. the composition-gradient copolymer gels were successfully prepared between hydrophilic and hydrophobic substrates. The gel prepared between T-T shows a convex distribution of AMPS content, decreasing in AMPS content near Teflon, similarly as the gel prepared between G-T. The gel prepared between G-G shows little concave distribution. Thus it could be said that hydrophilic AMPS is repulsed by hydrophobicity of Teflon wall and attracted by the hydrophilic glass surface. It is noted that the composition-gradient in the gel prepared between G-T is formed over the distance of "several millimeters". Although the reason is still unclear, the repulsion of AMPS to Teflon is considered to be a "trigger" for the formation of the composition-gradient gel with the distance of several millimeters. Osada et al. [4,5] reported that in the preparation of AMPS gel using hydrophobic wall, the polymer density was lower toward hydrophobic wall over the distance of several millimeters, which was interpreted in terms of the interfacial energy of polymer to wall and the osmotic pressure of the solution.

Figure 3 shows the photos of slab-shaped NIPA-*co*-AMPS gels in water at 7°C and 50°C. The gels were prepared under the conditions shown in Fig. 2 and those had the original size of 40 x 40 x 5 mm^3. It is well known that NIPA gel undergoes reversible swelling/shrinking in response to the temperature change due to the hydrophilic/hydrophobic transition. The copolymer gels prepared between G-G (Fig. 3 (b)) and T-T (Fig. 3 (c)) isotropically swelled and shrank in three directions as well as the case of the NIPA gel. On the other hand, the NIPA-*co*-AMPS gel prepared

between G-T (Fig. 3 (a)) underwent the anisotropic change in shape, i.e. bending at 50°C and stretching at 7°C. This thermosensitive change in shape was reversible without breaking through several times of the repeated temperature swing processes. This swelling pattern is explained as follows. In the copolymer gels, poly(NIPA) swells and shrinks with the change in temperature, but hydrophilic poly(AMPS) is kept at swollen state irrespective of the temperature. As shown in Fig. 2, the copolymer gel between G-T has the gradient composition in a direction perpendicular to the substrates, i.e. lower content of AMPS at the side of Teflon. Thus the shrinking degree of the Teflon-side gel at 50°C is larger than that of the glass-side gel, resulting in the bending. In addition to the gradient composition of the copolymer gel, the structural feature of the gel also contributes to the reversible and anisotropic change in the shape without breaking. It is well known that utilizing hydrophilic/hydrophobic transition, i.e., by polymerizing above the LCST in water, porous NIPA gel can be obtained [8]. The structure of NIPA-*co*-AMPS gel prepared at 40°C was porous, which was confirmed by the eye-observation that the gels are white as shown in Fig. 3. The porous NIPA gel can be deformed largely, since the shear modulus of porous gel is smaller than that of non-porous gel [8-10].

Figure 4 shows the contents of AMPS in slab-shaped NIPA-*co*-AMPS gels prepared at 40°C between G-T under the conditions that the concentrations of NIPA and AMPS in pre-gel solution were the sets of 1350/150 and 1455/45 mol/m^3, respectively. Solid and dot lines indicate the ideal values calculated from the concentrations in pre-gel solution. The observed values of AMPS contents were smaller than the ideal values for both gels. The lower conversion of AMPS is attributed to the lower reactivity of the copolymerization of NIPA and AMPS. In the literature [11], the reactivity ratios of NIPA (1) and AMPS (2) are $r_1 = 2.4$ and $r_2 = 0.03$, i.e., $r_1 r_2 = 0.072$. In the case of

higher concentration of AMPS, the remarkable composition-gradient NIPA-*co*-AMPS gel was obtained as the results of the increase in the conversion and the larger decrease in the AMPS content at Teflon side. The gel with higher concentration of AMPS largely bended at 50°C compared with the gel shown in Fig. 3 (a). Lowering of temperature to 7°C stretched the gel somewhat, but the gel was still arch-like.

Figure 5 shows the distributions of AMPS content in slab-shaped NIPA-*co*-AMPS gels, which were prepared between G-T at 25°C and G-G at 20°C. The concentrations of NIPA and AMPS were 1455 and 45 mol/m^3, respectively. The content of AMPS in the gel prepared between G-T at 25°C decreased toward Teflon as well as that in the gel prepared between G-T at 40°C, while the content of AMPS in the gel prepared between G-G showed negligible gradient dependence. Thus hydrophilic AMPS is repulsed by Teflon even in the media of hydrophilic poly(NIPA) at temperatures below the LCST. The slab-shaped NIPA-*co*-AMPS gel prepared between G-T at 25°C also bent at 50°C and stretched at 7°C in water similarly as shown in Fig. 3 (a). However, the gel was finally broken by repeating the temperature swing, which is explained as follows. The macroscopic structure of the gel prepared at 25°C was homogeneous, i.e. non-porous, which was visibly confirmed by the fact that the gel was transparent. When the homogeneous NIPA hydrogel undergoes the increase in temperature across the LCST, a skin layer on the gel surface is formed [12,13], resulting from the rapid shrinking at the surface. The dense and shrunken network around the gel surface prevents the interior water from diffusing into the outer solution. That resulted in the increase in interior pressure, which caused the crack.

Figure 6 shows the distributions of AA content in slab-shaped NIPA-*co*-AA gels prepared between G-T. Two kinds of the gels prepared with different concentrations of AA at 40°C were used. The ideal values calculated from the concentrations of AA in

pre-gel solution are shown by the solid and dot lines. AA distributes homogenously in NIPA-*co*-AA gels in contrast to NIPA-*co*-AMPS gels, although hydrophilic AA might be repulsed by Teflon. The difference in the distributions of ionic components in NIPA-*co*-AA and NIPA-*co*-AMPS gels comes from the reactivities of the ionic components. In NIPA-*co*-AA gels, the observed values of contents of AA corresponded to the ideal values. The higher conversion of AA is attributed to the good reactivity of the copolymerization of NIPA and AA. In the literature [11], the reactivity ratios of NIPA (1) and AA (2) are $r_1 = 14.0$ and $r_2 = 0.07$, i.e., $r_1 r_2 = 0.98$. In fact, the rate of the gelation of NIPA-*co*-AA was larger than that of NIPA-*co*-AMPS, where ca. two hours and ca. seven hours for the former and latter were taken to the time of approximate completion of gelation from the observation by eyes. In addition, the pH values in pre-gel solutions were 2.13 for NIPA-*co*-AA ([AA] = 50 mol/m^3) and 1.53 for NIPA-*co*-AMPS ([AMPS] = 45 mol/m^3), respectively. At these pH values, the amount of AA dissociated is little, while it is much for AMPS. Therefore, the non-dissociated AA can lead to the better reactivity of the copolymerization with NIPA and the lower repulsion to Teflon than those for dissociated AMPS.

The glass transition temperatures, T_gs, of NIPA-*co*-AA and NIPA-*co*-AMPS gels prepared in glass tube were measured to clarify the interaction of NIPA and ionic components. DSC curves for NIPA, AA and NIPA-*co*-AA gels and T_gs for those gels against the concentrations of AA in pre-gel solution are shown in Figs. 7 and 8, respectively. The values of T_gs of NIPA and AA gels were obtained as 134.2 and 130.0°C, respectively. The values observed for these gels are approximately the same as those reported for those polymers; 130°C [14] and 135°C [15] for NIPA polymer, and 126°C [14] and 95 – 129°C depending on molecular weight [16] for AA polymer. It should be noted that the values of T_gs of NIPA-*co*-AA copolymer gels were higher than

those of NIPA and AA gels. The value of T_g of a mixture composed of two components are generally intermediate between T_gs for each component. The larger values of T_g in NIPA-*co*-AA gels indicate the increase in their thermal stability, that is, NIPA and AA in NIPA-*co*-AA gels must be strongly interacting through hydrogen bonding with amide and carboxylic groups. Garay *et al*. [16] reported that T_gs of blends and complexes of NIPA and AA polymers at various compositions are higher than T_g of each polymer.

DSC analysis were also carried out for NIPA-*co*-AMPS gels prepared with various compositions and AMPS gel prepared in glass tube. The value of T_g of AMPS gel could not be determined from the DSC curve, which was non-inflexional, but Erdemi *et al*. [17] reported that T_g of AMPS polymer is 108°C. The value of T_g of copolymer gel containing a small amount of AMPS was approximately the same as that of NIPA gel. As the content of AMPS increased, the determination of T_g from the DSC curve became difficult. However, T_gs of NIPA-*co*-AMPS gels scarcely increased differently from NIPA-*co*-AA gels. Thus, there is no significant specific interaction between NIPA and AMPS in the gels. By taking account of the distributions of ionic components in slab-shaped NIPA-*co*-AA and NIPA-*co*-AMPS gels and the T_gs of both gels prepared in glass tube, it is essential for the preparation of a composition-gradient copolymer gel that the secondary component distributed interacts little with the primary component and is repulsed by a substrate, e.g. AMPS could not interact with NIPA and was repulsed by Teflon.

4. Conclusions

A thermosensitive primary component, NIPA, and an ionic secondary component,

AMPS or AA, between two substrates of hydrophilic glass and hydrophobic Teflon were copolymerized and the feasibility of the preparation of a novel composition-gradient copolymer gel was examined. In the NIPA-*co*-AMPS gels prepared at 40°C between glass and Teflon, the content of AMPS gradually decreased toward Teflon wall. The composition-gradient copolymer gel reversibly bended and stretched in response to the change in temperature. On the other hand, in the NIPA-*co*-AA gels prepared at 40°C between glass and Teflon, AA distributed homogeneously. Such a homogeneous distribution is attributed to the good reactivity and the strong interaction of NIPA and AA, which were explained in terms of the conversion and the glass transition temperature, respectively. To prepare a composition-gradient copolymer gel, it is essential that the secondary component is repulsed by a substrate and interacts little with the primary component.

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Figure captions

Fig. 1 Chemical structures of NIPA, AA and AMPS.

Fig. 2 Distribution of AMPS content in slab-shaped NIPA-*co*-AMPS gels prepared at 40°C between G-T, G-G and T-T. The concentrations of NIPA and AMPS in pre-gel solution were 1455 and 45 mol/m^3, respectively.

Fig. 3 Photos of slab-shaped NIPA-*co*-AMPS gels prepared at 40°C between (a) G-T, (b) G-G and (c) T-T in water at 7°C and 50°C. The concentrations of NIPA and AMPS in pre-gel solution were 1455 and 45 mol/m^3, respectively. The original sizes of the slab-shaped gels were 40 x 40 x 5 mm^3. In (a), upside of the gel is the glass-side and the length of upside arc is shown.

Fig. 4 Effect of concentrations of monomers in pre-gel solution on distribution of AMPS content in slab-shaped NIPA-*co*-AMPS gels prepared at 40°C between G-T.

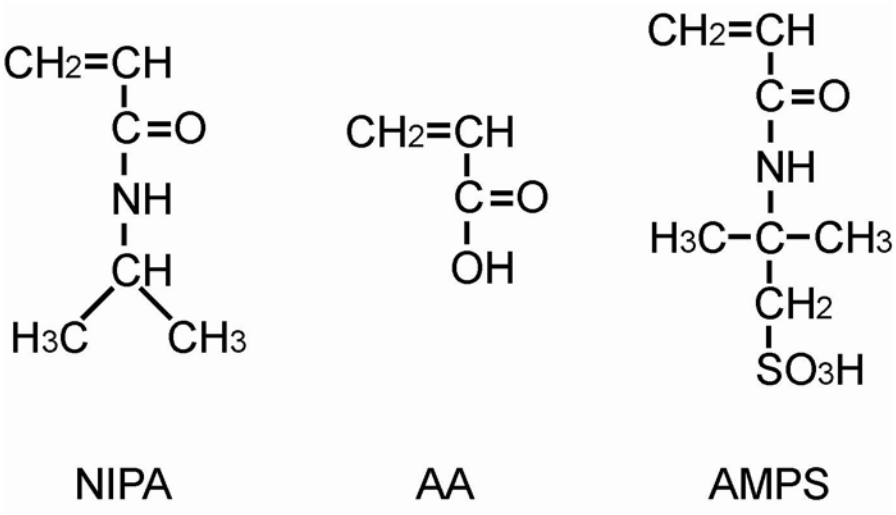
Fig. 5 Distribution of AMPS content in slab-shaped NIPA-*co*-AMPS gels prepared between G-T at 25°C and G-G at 20°C. The concentrations of NIPA and AMPS in pre-gel solution were 1455 and 45 mol/m^3, respectively.

Fig. 6 Distribution of AA content in slab-shaped NIPA-*co*-AA gels prepared at 40°C between G-T.

Fig. 7 DSC curves for NIPA, AA and NIPA-*co*-AA gels prepared in glass tube,

showing the T_gs. Absolute values for vertical axis were scrolled up and down for the easiness to see.

Fig. 8 Glass transition temperatures, T_gs, for NIPA, AA and NIPA-*co*-AA gels prepared in glass tube against the concentrations of AA under the condition of [NIPA] + [AA] = 1500 mol/m^3.



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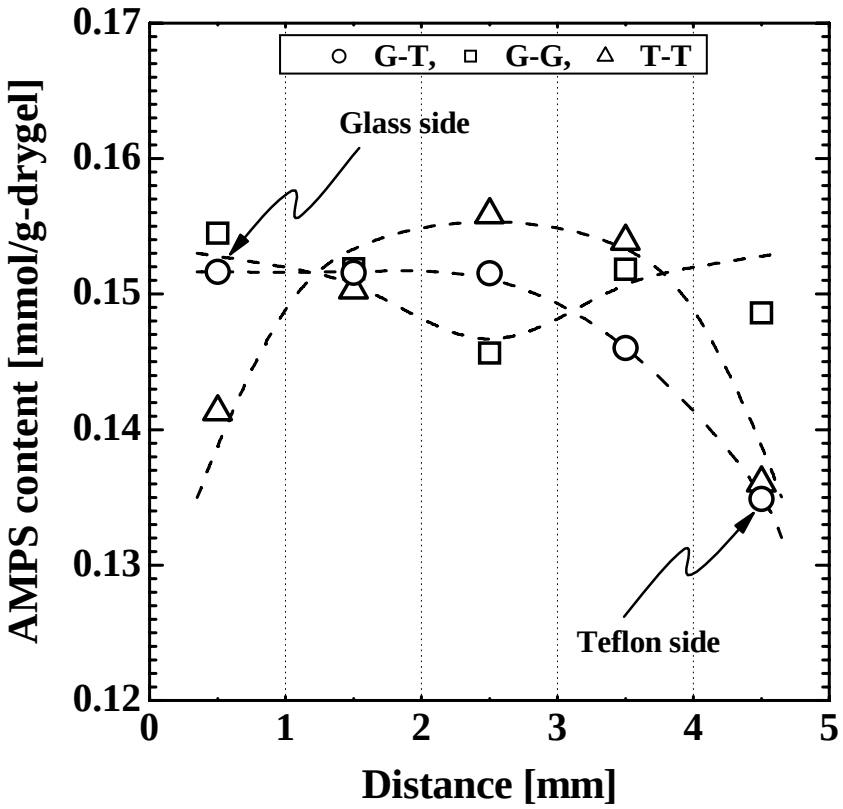

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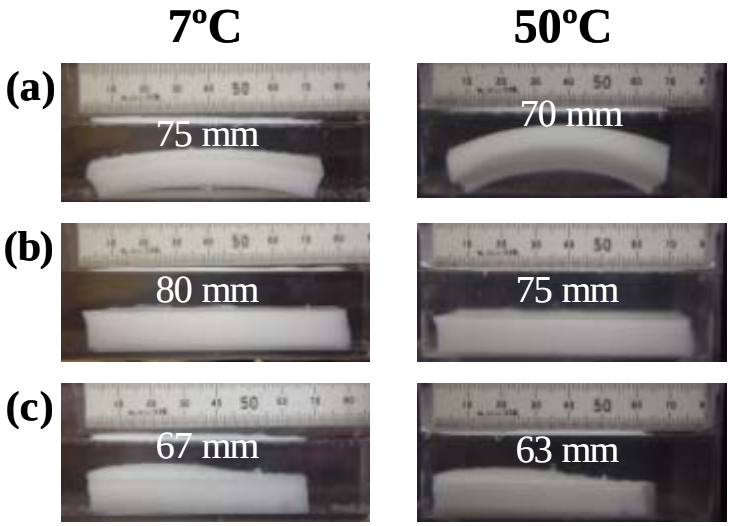

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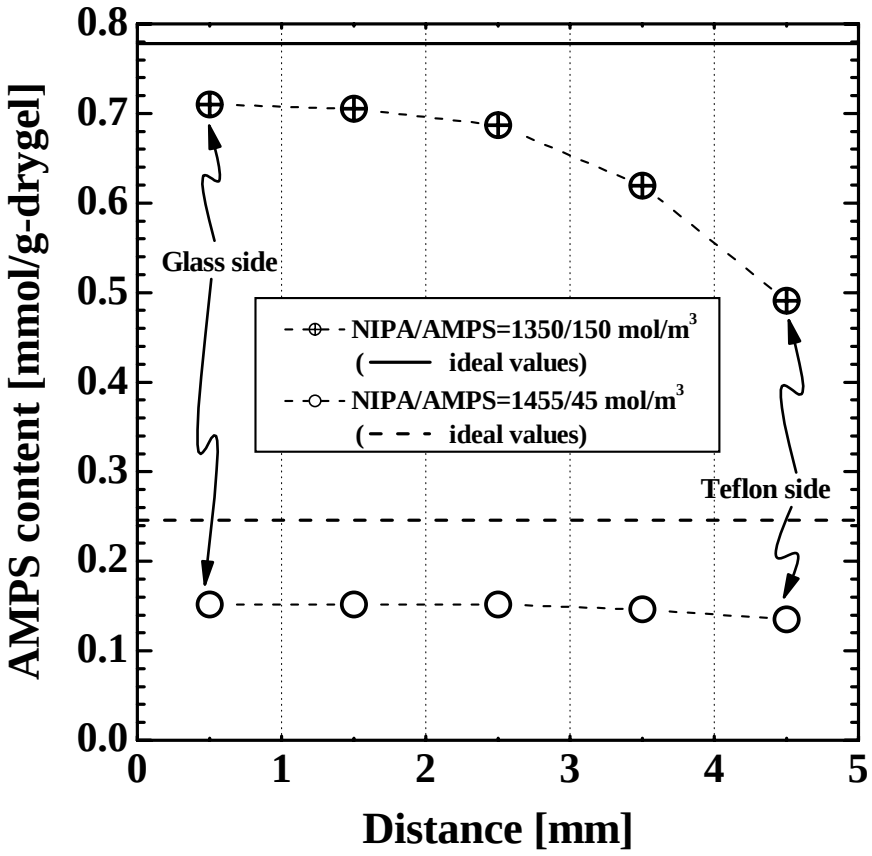

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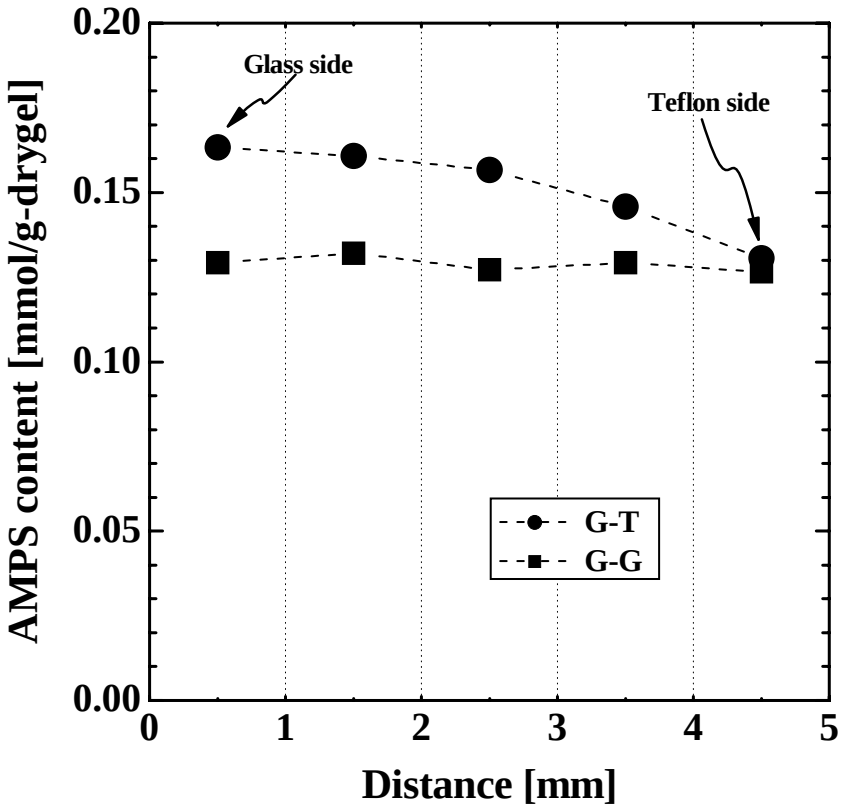

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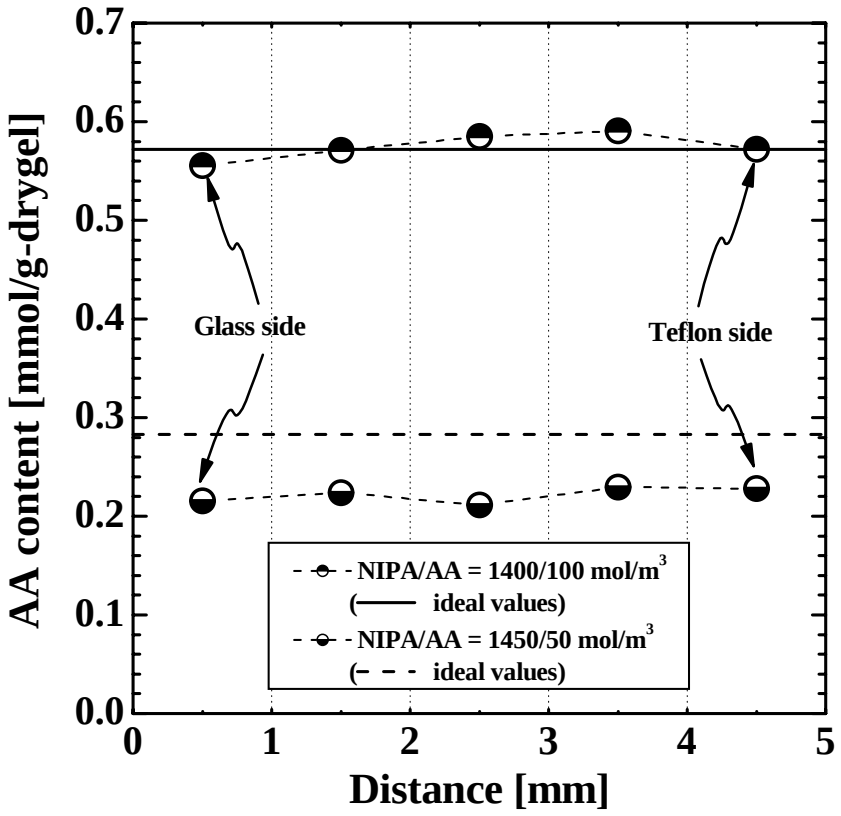

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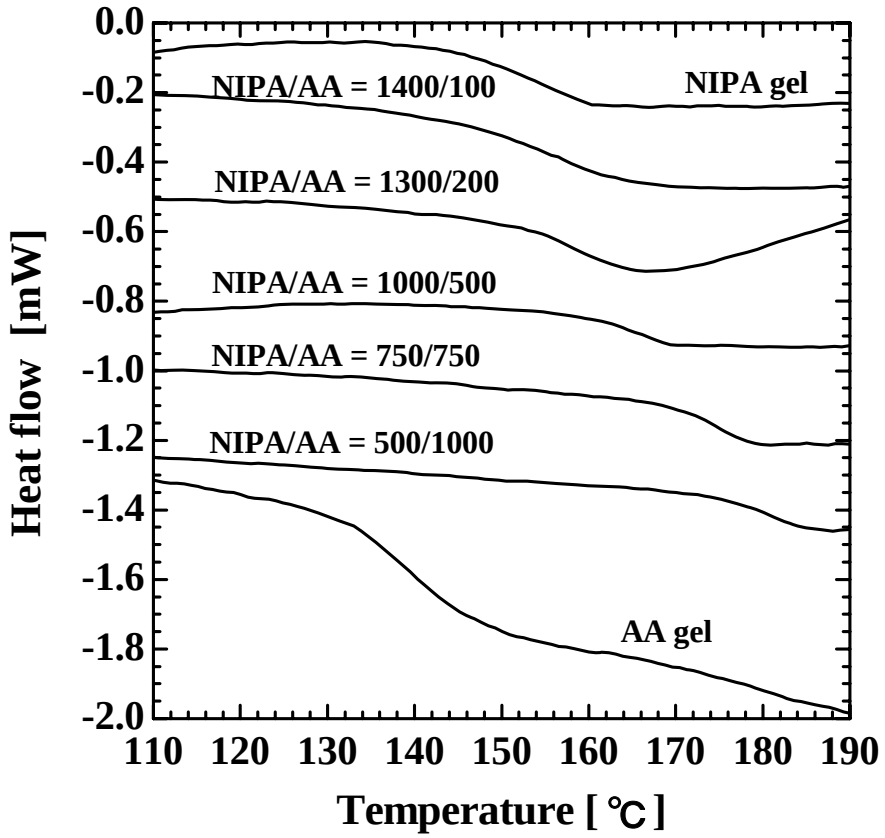

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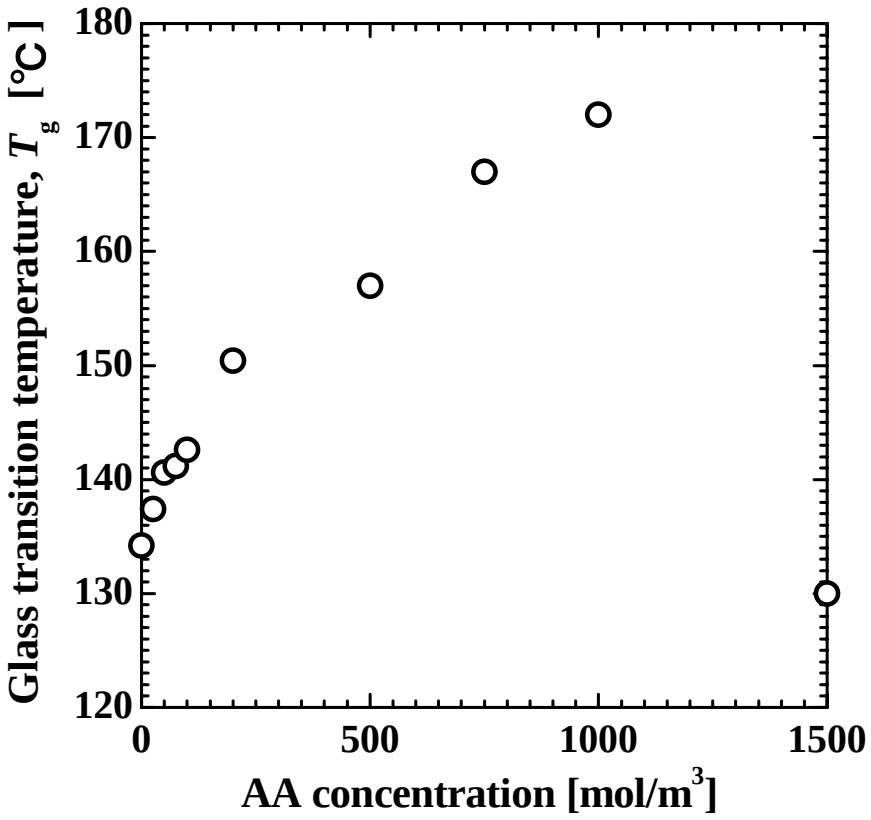

Figure 8, H. Tokuyama